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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,078	07/25/2001	William F. Wade	PM	7302

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,078	WADE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 7/6/06, is acknowledged.

Claims 1-31 had been canceled.

Claim 32 had been amended.

Claims 32-37 are pending and being acted upon presently.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.
This Action will be in response to applicant's amendment, filed 7/6/06.
The rejections of record can be found in previous Office Action, mailed 4/11/06.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 32-37 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.
The specification as originally filed does not provide support for the invention as now claimed:
"an adjuvant which induces a cytotoxic T lymphocyte response to the selected antigen of (i)" as recited in claim 32.

Applicant's amendment, filed 7/6/06, simply states that no new matter has been added, but does not provide sufficient direction to the written support in the specification as filed for this newly added limitation.

Applicant's apparent reliance on generic disclosure of "adjuvants" and inducing immune responses, including humoral immune response of Th1 immune response to target antigens (e.g. see Objects of the Invention on page 7 of the instant specification) does not provide sufficient direction and guidance to the particular class of adjuvants now recited in claim 32. Again, it is noted that the Objects of the Invention of the instant specification does not describe CTL responses and more particularly, do not mention the particular class of adjuvants now being claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Therefore, the specification as filed does not provide sufficient blazemarks or direction for the instant methods encompassing the above-mentioned "limitations" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.
See MPEP 714.02 and 2163.06

5. Claims 32-37 are rejected under 35 U.S.C.§ 103(a) as being unpatentable over Anand et al. (US 6,291,208 B1) and Heath (US 2002/0135722 A1) in view of Maraskovsky et al. (U.S. Patent No. 6,497,876) and Smith et al. (U.S. Patent No. 6,509,313) essentially for the reasons of record set forth in the previous Office Action, mailed 4/11/06.

Applicant's arguments, filed 7/6/06, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Applicant again maintains that the motivation to combine the cited reference is simply lacking because Anand et al. teach the disclosed conjugate antibody in the absence of conventional adjuvants.

It appears that applicant is asserting that the references, particularly Anand et al., is teaching away from the claimed methods.

It is noted that a prior art reference may be considered to teach away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." In re Gurley, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). General skepticism of those in the art -- not amounting to teaching away -- is also "relevant and persuasive evidence" of nonobviousness. Gillette Co. v. S.C. Johnson & Son, Inc., 16 USPQ2d 1923, 1929 (Fed. Cir. 1990). In effect, "teaching away" is a more pointed and probative form of skepticism expressed in the prior art.

Here in contrast to applicant's assertions of lack of motivation or teaching away by the prior art because one of the references indicates success without conventional adjuvants;

there is no discouragement nor skepticism in the prior art for combining adjuvants, including adjuvants which induce cytotoxic T lymphocyte responses against an antigen of interest in light of the totality of the prior art teachings to stimulate or enhance immune responses via antigen presenting cells such as dendritic cells to antigens of interest.

As pointed out previously and noted by applicant, it has been acknowledged that the prior art primary references do focus on the use of the described anti-CD40 antibody conjugates in the absence of adjuvants.

Also, noted previously and acknowledged by applicant,

Anand et al. teach the use of antibody conjugates comprising antibodies that bind antigen presenting cells, including dendritic cells to deliver antigens in order to generate immunogenic compositions to a variety of antigens that Heath teaches the co-administration of a CD40 stimulating moiety as an adjuvant in combination with an antigen.

As pointed out previously, Maraskovsky et al. has been added to provide additional teaching that for use in stimulating certain type of immune responses, administration of other cytokines along with antigen-pulsed dendritic cells (e.g. see Summary of the Invention, including column 2, paragraph 2 and Detailed Description, including column 11, paragraphs 3-4) (see entire document). It is noted that the dendritic antigen presenting dendritic cells taught by Maraskovsky et al. include stimulation via CD40, albeit via CD40L rather than the claimed anti-CD40 antibodies. In either case, clearly Maraskovsky et al. teach the presence of CD40 on antigen presenting cells, which can be targeted as well as the use of cytokines as adjuvants in efforts to enhance immune responses to antigens of interest at the time the invention was made.

Note, too, that the teaching of Heath indicates that the anti-CD40 antibody was an adjuvant in their system.

Also, note that Anand et al. teach that the recombinant conjugate when administered without an extrinsic adjuvant elicit good priming, but faded after a while and needed to be boosted (e.g. see column 8, paragraph 3).

Therefore, while Anand et al. does teach enhancing immune responses in the absence of conventional adjuvants, this teaching does not preclude the ordinary artisan to apply adjuvants, including combinations of certain types of adjuvants, such as cytokines, in boosting immune responses to antigens of interest.

For example, the prior art clearly provides for combination of cytokines in enhancing immune responses, as evidenced by Maraskovsky et al. (see Summary of the Invention, including column 2, paragraph 2 and Detailed Description, including column 11, paragraphs 3-4)

In addition, Smith has been provided to support he use of activating immune responses with cytokines, including combinations of cytokines to boost immune responses in the absence of toxicity (see entire document, Summary of the Invention and Detailed Description of the Invention).

Again, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Rather applicant appears to focus on certain aspects of Anand et al. and simply asserts that there was simply no motivation for use of the antibody conjugates to look for support for use with the teachings of Maraskovsky et al., Heath and Smith.

In contrast to applicant's assertions that there was little basis or motivation to combine the CD40 ligand adjuvant of Heath with the antibody conjugate of Anand et al. as well as comments concerning carrier system, the following of record is reiterated.

Anand et al. teach the use of antibody conjugates comprising antibodies that bind antigen presenting cells, including dendritic cells (e.g. column 2, paragraphs 4 and 6), to deliver antigens in order to generate immunogenic compositions to a variety of antigens (e.g. column 7, paragraph 2) (see entire document, including Summary of the Invention and General Description of the Invention). Anand et al. Teach that these is applicable to any antigen which it is desired to target to antigen presenting cells, including antigens derived from viruses, bacteria and tumors (see column 7, paragraph 1)

Heath teaches the co-administration of a CD40 stimulating moiety (e.g. anti-CD40 antibodies) (e.g., see paragraphs 0055, 0061, 0062) and the appropriate antigen, including the use of covalent linkage or co-entrapment as a vaccine (e.g. see paragraphs 0026-0027 and 0029) to a variety of antigens (see entire document, including Summary of the Invention).

Maraskovsky et al. has been added to provide additional teaching that for use in stimulating certain type of immune responses, administration of other cytokines along with antigen-pulsed dendritic cells (e.g. see Summary of the Invention, including column 2, paragraph 2 and Detailed Description, including column 11, paragraphs 3-4) (see entire document). It is noted that the dendritic antigen presenting dendritic cells taught by Maraskovsky et al. include stimulation via CD40, albeit via CD40L rather than the claimed anti-CD40 antibodies. In either case, clearly Maraskovsky et al. teach the presence of CD40 on antigen presenting cells, which can be targeted as well as the use of cytokines as adjuvants in efforts to enhance immune responses to antigens of interest at the time the invention was made.

Given the teachings of Heath to provide anti-CD40 with antigen in composition form or as a conjugate (see Summary of the Invention) and the teachings of Anand et al. to provide antigen with anti-antigen presenting cell / dendritic cell antibodies; it would have been obvious to one of ordinary skill in the art to administer the antigen in the context of such antigen-antibody conjugate with the immunostimulatory anti-CD40 antibodies to boost the immune response to a wide variety of desired antigens, including providing both components in the same composition, as taught by Heath (see paragraphs 0026-0027 and 0029).

In addition, the motivation to combine the prior art can arise from the expectation that the prior art elements will perform their expected function to achieve their expected results when combined for their common known purpose. Here, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine both antigen-antibody conjugates for dendritic cells and CD40-specific antibodies to target antigens to the antigen presenting cells of interest, including CD40-expressing antigen presenting cells, as well as to enhance the immunogenicity of said antigens.

Given the teachings of Anand et al. and Heath; the ordinary artisan would have been motivated to target professional antigen presenting cells such as dendritic cells with the combination of antigen-antibody targets and the immunostimulatory agonistic CD40 antibodies to enhance the immune response to a wide variety of antigens. As routinely practiced at the time the invention was made, adjuvants were employed to boost immune responses to antigens of interest. Both Maraskovksy et al. and Smith teach the known use of cytokines to boost immune responses to antigens of interest, including the advantages of using cytokines in low toxicity formulations, consistent with the teachings of Heath, who teaches advantages of low toxicity formulations of anti-CD40 immunoconjugates in boosting immune responses. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

6. No claim allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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September 7, 2006